

만성중이염 환자와 정상성인에서 공기 온도안진검사의 신뢰성

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Reliability of Air Caloric Response in Healthy Volunteers and Patients With Chronic Otitis Media

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Background and Objectives: To investigate reliability of the air caloric test compared to the water caloric test and to determine whether anatomical alterations due to chronic otitis media (COM) influence air caloric response. **Materials and Methods:** Fifty-six subjects without vestibulopathy (24 healthy individuals as control group and 32 patients with unilateral COM as experimental group) were included. The bithermal water and air caloric test were sequentially conducted in control group. The bithermal air caloric tests, high-resolution temporal bone computed tomography and endoscopic photography of the ear drum were obtained from experimental group. **Results:** Although maximal slow phase velocities and time to reach peak velocity using water irrigation were significantly higher and shorter, respectively, than those by air irrigation in normal subjects, caloric parameters on air caloric test agreed well with those of water caloric testing. However, inverted nystagmus occurred in 16 ears of 16 subjects, which was predominantly presented during warm air stimulation in the com patient group. The large tympanic membrane perforation and asymmetrical mastoid pneumatization were significant parameters affecting caloric response. The presented prediction model for cold-induced mspvs corresponded with observed values according to mastoid pneumatization. **Conclusion:** Although the air caloric stimuli resulted in a reliable response in healthy subjects, air caloric results among com patients affected by anatomical alteration as well as irrigation temperature. Presented mathematical model for cold induced mspv could serve as a good reference in measuring true vestibular function in com patients.

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Key Words: Caloric test; Air; Otitis media; Reliability

INTRODUCTION

The caloric test has been widely used to identify asymmetry in the peripheral vestibular system by separately stimulating each ear. Since a variety of caloric test protocols have been introduced into clinical practice, the American National Standard Institute and British Society of Audiology defined the alternative bithermal caloric test protocol using water irrigation in 1999 as a recommended caloric test procedure.

However, the caloric test, using air as the thermal conduction medium, in situations when water is not applicable, has not become standardized despite its common clinical use because it is more technically demanding to ensure reliability and greater inter-subject variability are usually observed.¹ Furthermore, changes in thermal conduction from the ear canal to the inner ear could occur in cases with an anatomical alteration such as chronic otitis media (COM).²⁻⁵ As a result, it is questionable whether the results of the caloric test are measuring true vestibular asymmetry or asymmetrical thermal transmission due to an anatomical alteration.

In this study, we investigated the equivalence of the caloric response induced by water and air media in healthy subjects. We also determined whether results of air caloric response in patients with COM are predictable and reliable for identifying true vestibular function.

MATERIALS AND METHODS

1. Subjects

Fifty-six subjects, 24 healthy volunteers (6 men and 18 women, mean age, 40±12 years) as a control group and 32 patients with unilateral COM without an active ear discharge (12 men and 20 women, 49±11 years) as the patient group, were recruited. Approval for this study was obtained from the institutional review board at Seoul National University Bundang Hospital.

Inclusion criteria for normal subjects were: 1) no history of vertigo or ear surgery, 2) head shaking nystagmus <2°/sec and a normal head impulse test, and 3) no history of medication of ototoxic agent use. Among COM patients who met these criteria, patients who had the same bone conduction threshold in the perforated ear compared to that of the healthy side at the

pure tone octave frequency of 500-4,000 Hz were included as the patient group. No statistically significant differences were observed for gender or age between the two groups.

2. Methods

The bithermal alternating caloric test was performed in the control group using water and air irrigation at two days interval. The bithermal alternating caloric test using water irrigation is described in detail elsewhere. Briefly, the test was performed in the supine position with the head elevated 30° using a NCI480 water caloric stimulator (ICS Medical, Schaumburg, IL, USA). The order of irrigation was right cool, left cool, right warm, and then left warm. Each irrigation was conducted for 30 seconds with a flow rate of 300 mL/min for cold (30°C) or warm (44°C) water. The air caloric test was performed in a similar manner using a NCA-200 air caloric stimulator (ICS Medical). Each irrigation was performed for 50 seconds with a flow rate of 10 liter/min using warm (50°C) or cold (24°C) air. Maximal slow phase velocities (MSPVs) and time to reach peak velocity under each test condition were compared between the two methods.

The bithermal air caloric test was performed in the patient group. Endoscopic photographs were taken of the tympanic membrane on the perforated side to measure perforation size, which was calculated relative to the whole tympanic membrane using the IMPAX program (AGFA Healthcare, Mortsels, Belgium). High-resolution temporal bone computed tomography (collimation, 4×0.75 mm; slice thickness, 0.75 mm; high resolution mode; 250 mA and 120 kVp per slice) was performed to investigate anatomical alterations of the middle ear space and mastoid bone using the MX8000-IDT system (Phillips Medical Systems, Best, the Netherlands). The air-space volumes in the middle ear and mastoid bone were calculated using a three-dimensional (3D) rendering program (Rapida, Infinitt Healthcare System, Seoul, Korea).

The inter-aural difference (IAD) ratio was calculated by:

$$\frac{[\text{Air volume of healthy side} - \text{Air volume of affected side}]}{\text{Air volume of healthy side} + \text{Air volume of affected side}}$$

The following anatomical variables were used for comparison:

1) Tympanic membrane perforation ratio (TMPR), 2) IAD ratio of mastoid air volume (MA), 3) IAD of middle ear air volume

(MEA).

3. Statistical analysis

The caloric test parameters of the MSPVs for each condition, time to reach peak velocity, canal paresis (CP), and directional preponderance (DP) obtained by air irrigation were compared with those of water irrigation using the paired *t*-test in the control group. A descriptive statistical analysis such as the geometric mean, standard deviation (SD), and reference intervals (RI) were used to estimate the distribution of MSPVs for water and air stimuli under both warm and cold temperatures. In addition, the Bland-Altman analysis was used to evaluate substantial agreement between the air and water caloric test.

Caloric parameters obtained by air irrigation were analyzed in the patient group. Iterative algorithms were used to test the correlation between the IAD ratio of the MSPVs and the IAD ratio of anatomical alteration. All statistical analyses were conducted using SPSS ver. 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Non linear curve fitting using iterative algorithms was performed with OriginPro 8.1 (OriginLab Corporation, Northampton, MA, USA).

RESULTS

1. Comparison of caloric response between air irrigation and water irrigation in healthy subjects

MSPVs induced by water irrigation were higher than those induced by air irrigation under the four conditions. Paired comparisons between these water and air caloric test parameters

under the same conditions showed statistically significant differences ($p<0.05$). In contrast, no significant differences were observed for CP and DP between the two irrigation methods (Table 1). Time to reach peak velocity by water irrigation was shorter than that by air irrigation using both cold and warm stimuli ($p<0.05$) (Table 2). Based on these findings, we investigated substantial agreement between the two tests using a Bland-Altman plot, which is designed to measure whether the same parameter is correlated.⁶ Differences in CP and DP between the water and air caloric tests were within the mean \pm 1.96 SD, indicating that the two tests can be used interchangeably (Figure 1).

The geometric mean and estimated RI of the MSPV from the modeled probability distributions for the water and air stimuli were calculated to establish differences between the distribution of water and air caloric induced MSPVs (Table 2). Air and water irrigation with a cold temperature resulted in a

Table 1. Comparison of maximal slow phase velocity, canal paresis and directional preponderance between water irrigation and air irrigation in healthy group

	Water	Air	<i>p</i> -value*
Right warm (deg/sec)	31 \pm 12	25 \pm 9	0.01
Right cold (deg/sec)	33 \pm 12	24 \pm 10	<0.001
Left warm (deg/sec)	35 \pm 16	25 \pm 12	<0.001
Left cold (deg/sec)	30 \pm 12	24 \pm 9	<0.001
Summation (deg/sec)	131 \pm 43	99 \pm 35	<0.001
Canal paresis (%)	7.9 \pm 5	8.4 \pm 6	0.78
Directional preponderance (%)	9.4 \pm 5.6	8.3 \pm 6	0.81

*Paired *t*-test.

Table 2. Geometric mean values and reference interval of maximal slow phase velocities and time to reach peak velocity on 48 healthy ears for water and air irrigation

	Cold		Warm	
	Air	Water	Air	Water
Geometric mean of MSPV (deg/sec)	23.34	29.24	22.61	26.65
90% RI (deg/sec)	10.01-40.43	16.60-51.49	11.64-43.90	13.54-52.43
95% RI (deg/sec)	10.28-52.99	14.90-57.39	10.25-49.85	11.89-59.68
99% RI (deg/sec)	7.94-68.57	12.05-70.93	8.00-63.91	9.23-76.89
Time to reach a peak velocity (sec)	83 \pm 10	72 \pm 11	82 \pm 10	78 \pm 8

MSPV, maximal slow phase velocity; RI, reference interval.

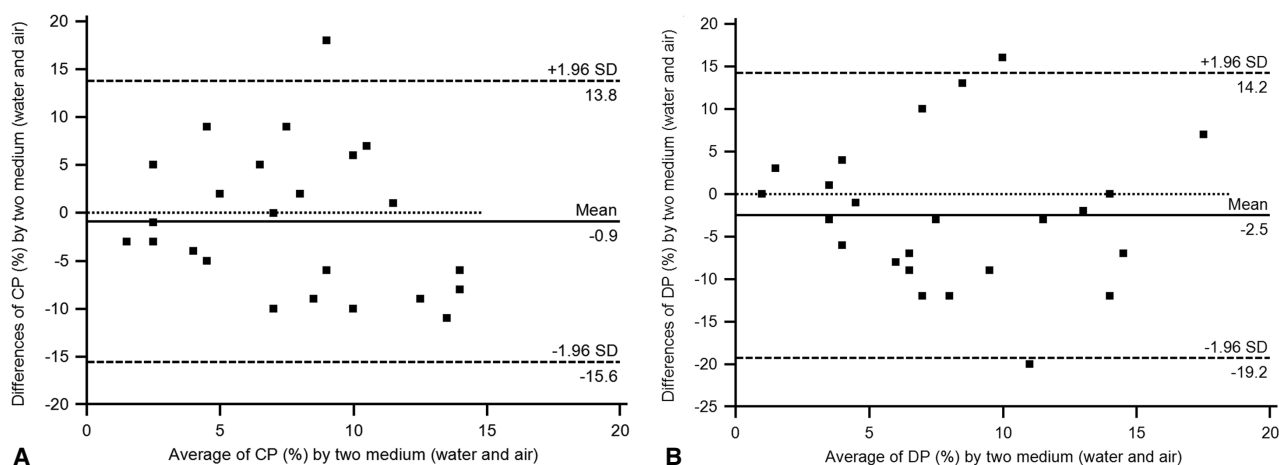


Figure 1. Bland-Altman plot of CP (A) and DP (B) between air and water stimuli. The majority of the difference of CP and DP between two methods fall within mean \pm 1.96 SD of the differences, indicating that the two irrigation methods can be used interchangeably. CP, canal paresis; DP, directional preponderance; SD, standard deviation.

hyperactive response when the MSPV was $>69^{\circ}/\text{sec}$ and $71^{\circ}/\text{sec}$, respectively, at 99% RI. However, the hyperactive response following air and water irrigation using warm temperature were $>64^{\circ}/\text{sec}$ and $77^{\circ}/\text{sec}$, respectively, and at the same statistical level, indicating that the limit of the hyperactive response was more varied according to irrigation type under warm temperature.

2. Air caloric response according to anatomical factors in the patient group

1) Caloric inversion vs. anatomical alteration in all patients (n=32)

Caloric inversion (inverted nystagmus) was present in 16 perforated ears during air caloric stimulation. Fifteen of 16 ears were induced by warm air stimulation, whereas the remaining one was induced by cold air stimulation. TMPR showing caloric inversion ($36\pm 20\%$) was higher than that without caloric inversion ($22\pm 14\%$) and was statistically significant. In contrast, the IAD ratio of MA and MEA had no influence on caloric inversion (Figure 2).

2) A comparison of the response between cold and warm irrigation in patients with a normal caloric response (n=16)

The two distributions of the observed MSPVs following warm and cold air irrigation were nearly identical in the 16

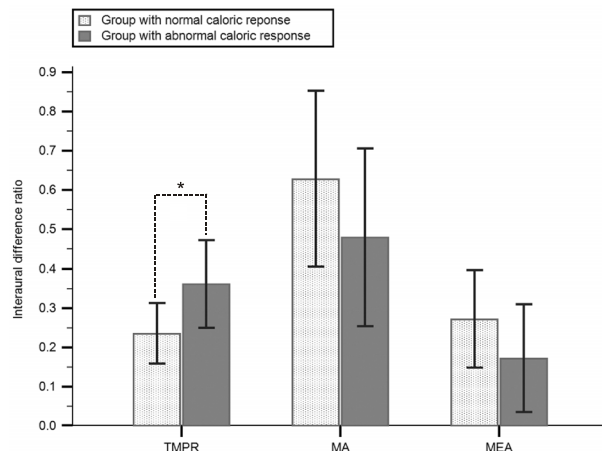


Figure 2. Comparison of anatomical factors between patients with a normal caloric response and those with an abnormal caloric response. The perforation ratio of patients with an abnormal caloric response was significantly greater than that of patients with normal caloric response ($p=0.028$). TMPR, tympanic membrane perforation ratio; MA, mastoid air volume; MEA, middle ear air volume.

patients with a normal caloric response. However, there was a tendency for cold air irrigation to show higher MSPVs than those induced by warm air irrigation (Figure 3). Additionally, no differences in cold-induced MSPV were observed between intact ($29\pm 19^{\circ}/\text{sec}$) and perforated ears ($27\pm 23^{\circ}/\text{sec}$), whereas MSPVs ($17\pm 17^{\circ}/\text{sec}$) induced by warm air irrigation on the perforated side were significantly lower than those ($27\pm 24^{\circ}/\text{sec}$) on the intact ear side ($p<0.05$) (Figure 4).

3) Caloric response prediction model in the presence of an anatomical alteration in all patients (n=32).

After air cell volume of the mastoid and middle ear cavity was calculated using a 3D rendering program (Rapida, Infinitt Healthcare System), we performed a correlation test between IAD of the air volume and that of cold-induced MSPVs using an iterative algorithm for nonlinear equations (analysis of warm induced MSPV was not performed due to its unstable response). The logistic equation is presented as a model fit to predict caloric response according to anatomical alterations.

The logistic equation is:

$$y = A_2 + \frac{A_1 - A_2}{1 + (x/x_0)^p}$$

The curve of the cold-induced MSPVs (iterations, 372; reduced x^2 , 0.017; fit converged-tolerance criterion satisfied) according to the MA IAD ratio was compatible with this logistic equation model (parameter $A_1=0.05$, $A_2=1.49$, $x_0=258151.92$, $p=0.18$) (Figure 5). The MSPV value from the

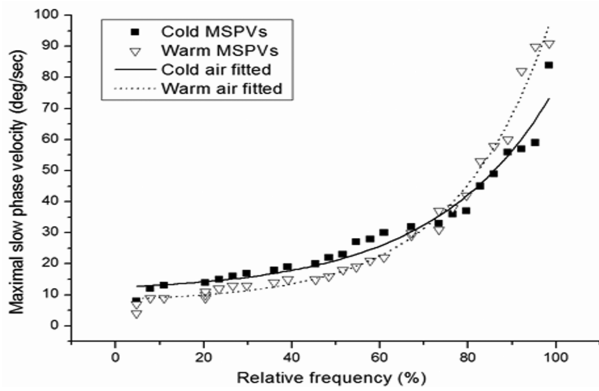


Figure 3. Comparison of cold-induced maximal slow phase velocities (MSPVs) and warm induced MSPVs in patients with a normal caloric response (n=16, 32 ears). Symbols and lines correspond to observed data and the fitted curve, respectively, according to the logistic model. Cold irrigation showed a stronger response than that of warm irrigation.

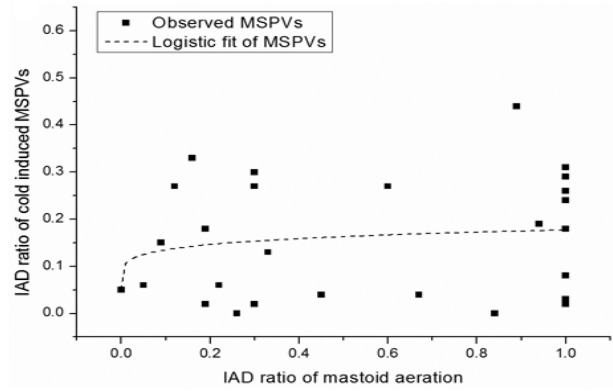


Figure 5. Plots of the model fit curve and observed inter-aural difference (IAD) ratio of cold-induced maximal slow phase velocities according to the mastoid air volume IAD ratio. Squares and dotted line represent observed IAD values of cold-induced maximal slow phase velocities (MSPVs) and a curve fit by logistic equation using an iterative algorithm, respectively.

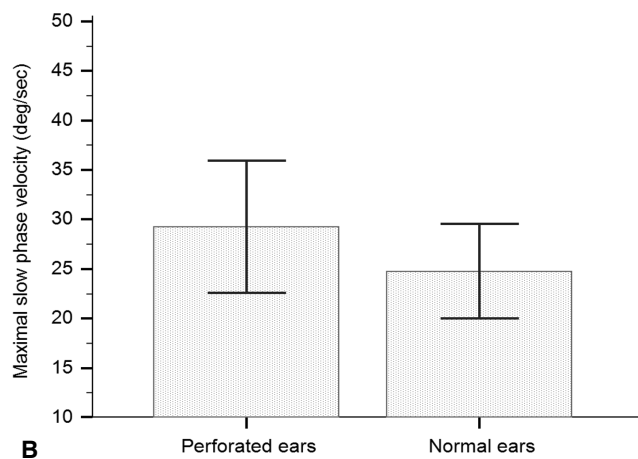
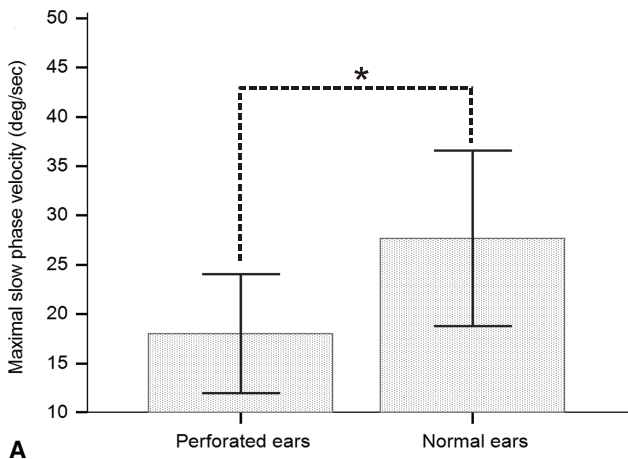


Figure 4. Comparison of maximal slow phase velocities (MSPVs) according to air irrigation temperature in patients with a normal caloric response (n=16, 32 ears). Significantly higher MSPVs were observed in normal eardrums when compared to those in perforated eardrums using warm air irrigation ($p=0.032$, A), whereas no statistically significant difference in MSPVs was observed between perforated and normal eardrums following cold air irrigation (B).

Table 3. The theoretical results of model prediction for cold induced maximal slow phase velocity and observed results

IAD ratio of MA	Theoretical IAD ratio of cold induced MSPV	Observed IAD ratio of cold induced MSPV
0.19	0.145	0.18
0.33	0.153	0.13
0.94	0.175	0.19
1	0.177	0.24

IAD, inter-aural difference; MA, mastoid air volume; MSPV, maximal slow phase velocity.

model prediction curve is compared to our observed results in Table 3. The IAD of ME and TMPR did not influence the IAD of cold-induced MSPVs.

DISCUSSION

Our major concern was to investigate whether the air caloric test could provide useful information to identify vestibular asymmetry as in the water caloric test. Many authors have reported that air as a caloric medium is more convenient to apply in adults or children who have an intolerance for water irrigation and it is a suitable alternative to water.^{4,7-10} In contrast, air stimulation does not produce a robust caloric response compared to that of water stimulation because it is a poor thermal conductor.¹¹ Moreover, it is technically more demanding to ensure reliable results, and greater inter-subject variability is occasionally observed.^{8,10} We thought that a careful comparative analysis between the water and air caloric test was the first step to investigate the reliability of the air caloric response in healthy subjects. Our results showed that air caloric stimulation provoked a weak response compared to that of water caloric stimulation (Table 1). Table 2 presents the geometric means of the MSPVs and the RI data from the modeled probability distributions for the water and air stimuli. Water stimuli tended to provoke stronger MSPVs than those of air stimuli and time to reach peak velocity by air irrigation was also longer than that by water irrigation under both warm and cold temperature. These findings corresponded well with an earlier study that water irrigation provokes a more robust response.¹¹ However, no significant differences were observed for CP or DP using the Jongkees formula between the two

irrigation methods and the variability around the geometric mean was fairly similar across the different irrigation types and temperatures, indicating that the two methods have similar diagnostic reliability to examine vestibular status.

On the other hand, no difference in the degree of hyperactive response was observed between the two air irrigations (69°/sec) and the water irrigations (71°/sec) at 99% RI under cold temperature. However, the hyperactive response by air and water irrigation under warm temperature was calculated to be 64°/sec and 77°/sec, respectively, at the same statistical level, suggesting that it could be more reliable to identify a hyperactive response from cold irrigation than that of warm irrigation due to the large variability in the level indicating a hyperactive response between air and water irrigation using warm temperature (Table 2).

Based on these findings, we used the Bland-Altman method for assessing the substantial agreement between parameters from the two caloric tests in the same subjects. The Bland-Altman analysis, even if there is compelling evidence of its importance, has been used as a graphical method that determines whether two tests can be used interchangeably in numerous published clinical studies. The concept is to calculate the mean difference between two tests of measurement (the bias) and 95 % limits of agreement as the mean difference or more precisely 1.96 SD. The majority of the difference value of CP and DP between two methods fall within mean±1.96 SD of the differences, indicating that the two irrigation methods can be used interchangeably.^{6,12}

Second, we analyzed the air caloric test results in relation to anatomical alterations in patients with unilateral COM. In contrast to the results of healthy subjects, large inter-subject and intra-subject variability in the caloric response was observed, particularly for the difference in caloric response between perforated and normal ear drums in patients. In our study, caloric inversion was found in 16 perforated ears in patients with COM, which predominantly occurred during warm air stimulation (15/16, 93%), suggesting that the response resulted mainly from the cooling effect due to evaporation in perforated ears.¹³ Warm air flow in contact with moist mucosa creates a cooling effect due to evaporation, and this colder temperature was transmitted to the endolymph, producing nystagmus on the side opposite to what was expected.⁵ Our results also showed that the tympanic perforation ratio is an

important anatomical factor resulting in caloric inversion (Figure 4). These results correspond with an earlier study concluding that inverted caloric response by warm air irrigation could occur in patients with a large perforation or mastoidectomy cavity.² However, the IAD of MA and MEA did not influence caloric inversion.

We investigated caloric parameters induced by different temperatures in patients with a normal caloric response (n=16). A tendency for cold air irrigation to show higher MSPVs was observed compared to those induced by warm air irrigation, which was analogous to caloric responses in normal healthy subjects. No IAD of the MSPVs and time to reach peak velocity was observed between the perforated ear and normal ear following cold air irrigation, which was thought to be associated with the absence of thermal stimulation distortion, because cold stimulation acts more strongly on the skin of the external auditory canal than warm stimulation, regardless of anatomical alteration.⁹ However, the MSPV distribution itself following the warm and cold air irrigations was well adapted to the logistic fit model, indicating that air caloric test show reliable and predictable results if patients with COM show a normal caloric response without caloric inversion under all conditions.

We finally performed a statistical analysis between IAD of the air volume and IAD of cold-induced MSPVs to predict a caloric response under the presence of anatomical alteration in all patients (analysis of warm-induced MSPV was not performed due to the unstable response). We used an iterative algorithm, which is a mathematical procedure to develop a desired model. The logistic fit model to predict IAD of cold-induced MSPVs according to anatomical alteration is:

$$y = A_2 + \frac{A_1 - A_2}{1 + (x/x_0)^p}$$

The observed IAD of cold-induced MSPV according to the MA IAD ratio was well adapted to this logistic model (iterations, 372; reduced chi-square, 0.017; fit converged-tolerance criterion satisfied). If, y=IAD ratio of cold-induced MSPV and x=IAD ratio of MA, then Parameter $A_1=0.05$, $A_2=1.49$, $x_0=258151.92$, $p=0.18$.

The theoretical results of this prediction model for cold-induced MSPV compared to the observed results are

shown in Table 3.

CONCLUSION

While the response to air irrigation was less than that of water irrigation, the air caloric test showed a reliable response. However, the bithermal air caloric test in patients with middle ear disease did not represent the vestibular status of the patient appropriately. Therefore, we must carefully review the raw data and consider anatomical alterations according to the presented mathematical model. Additionally, this mathematical model for cold induced MSPV could serve as a good reference in measuring true vestibular function in COM patients.

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중심 단어: 온도 안진검사, 공기, 중이염, 신뢰도

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